Appl. No.: 10/007,257 Filed: 11/12/2001

Page 2

Amendments to the Claims:

1. (Currently Amended) Water soluble particles of less than 50 μm comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon; wherein said coprecipitant has a molecular weight of less than 1,000 Da

wherein the coprecipitant is selected from the group consisting of

inorganic salts,

sugars, polysaccharides, polyols, and derivatives thereof with a molecular weight of less than 10,000 Da;

amino-acids;

acid-base buffers;

zwitterionic compounds;

organic salts;

compounds containing multiple basic groups;

compounds containing multiple acidic groups;

bile salts; and,

water soluble dyes.

- 2. (Original) Water soluble particles according to claim 1 wherein the coprecipitant core is partially or substantially crystalline.
- 3. (Original) Water soluble particles according to claim 1 wherein the dehydrated biological macromolecule is selected from peptides, polypeptides, proteins and nucleic acid.
- 4. (Original) Water soluble particles according to claim 1 having a diameter less than $10 \, \mu m$.
 - 5. (Canceled)

Appl. No.: 10/007,257 Filed: 11/12/2001

Page 3

- 6. (Currently Amended) A method of preparing water soluble particles comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon wherein said coprecipitant has a molecular weight of less than 1,000 Da comprising the steps of:
- a) preparing an aqueous solution comprising a coprecipitant and a biological macromolecule wherein the coprecipitant is selected from the group consisting of inorganic salts; sugars, carbohydrates, polyols, and derivatives thereof with a molecular weight less than 10,000 Da; amino-acids; acid-base buffers; zwitterionic compounds; organic salts; compounds containing multiple basic groups; compounds containing multiple acidic groups; bile salts; and, water soluble dyes wherein said coprecipitant has a molecular weight of less than 1,000 Da;
- b) rapidly admixing the biological macromolecule/coprecipitant solution with an excess of a water miscible organic solvent such that the coprecipitant and bioactive molecule immediately coprecipitate from solution forming said particles; and
 - c) isolating said particles from the organic solvent.
- 7. (Currently Amended) The method according to either of claim 6 or 42 wherein the aqueous solution comprising the coprecipitant and the biological macromolecule is prepared by dissolving the coprecipitant in an aqueous solution comprising the biological macromolecule.
- 8. (Previously Presented) The method according to claim 6 wherein the biological macromolecule/coprecipitant solution is added to the water miscible organic solvent.
- 9. (Original) The method according to claim 6 wherein the coprecipitant biological macromolecule molar ratio is greater than 50.
 - 10. (Canceled)
- 11. (Original) The method according to claim 6 wherein the organic solvent is selected from methanol, ethanol, propanol, acetonitrile, tetrahydrofuran and acetone.
 - 12. (Original) Particles obtainable by the process according to claim 6.

Appl. No.: 10/007,257

Filed: 11/12/2001

Page 4

13. (Currently Amended) A pharmaceutical formulation comprising particles according to claims 1 or 12 and a suitable carrier therefore.

- 14. (Original) A medical device comprising particles according to claims 1 or 12 associated therewith.
 - 15. (Original) Particles according to claims 1 or 12 for use in therapy.
- 16. (Original) A biocatalyst preparation comprising particles according to claims 1 or 12 associated therewith.
- 17. (Original) A cleansing agent comprising enzyme coated particles according to claims 1 or 12.
- 18. (Original) A protective or antifouling agent comprising particles according to claims 1 or 12 in association with paint, varnish, coatings or films.
- 19. (Original) Films, polymers, inks, coatings, electrodes and optical materials for diagnostic kits or biosensor applications, comprising particles according to claims 1 or 12.
- 20. (Original) A method for studying molecular recognition, molecular binding, molecular imprinting or inhibitor binding in non-aqueous media, comprising using particles according to claims 1 or 12.
- 21. (Original) A method for studying macromolecule structure and/or organisation by scanning probe microscopy, comprising using particles according to claims 1 or 12.
- 22. (Currently Amended) A method of isolating a biological macromolecule from an aqueous solution, comprising the steps of:

Appl. No.: 10/007,257 Filed: 11/12/2001

Page 5

- a) preparing an aqueous solution comprising a mixture of a coprecipitant and biological macromolecule to be isolated wherein said coprecipitant has a molecular weight of less than 1,000 Da; and
- b) admixing the biological macromolecule/ coprecipitant solution with an excess of a water miscible organic solvent such that the coprecipitant and biological macromolecule immediately coprecipitate from solution to form water soluble particles of less than 50 μm and having a coprecipitant core with a dehydrated biological macromolecule coated thereon, with rapid simultaneous dehydration of the biological macromolecule.
- 23. (Currently Amended) Water soluble particles of less than 50 µm comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon wherein said coprecipitant has a molecular weight of less than 1,000 Da obtainable by:
- a) preparing an aqueous solution comprising a coprecipitant and biological macromolecule wherein said coprecipitant has a molecular weight of less than 1,000 Da; and
- b) admixing the biological macromolecule/ coprecipitant solution with an excess of a water miscible organic solvent such that the coprecipitant and biological macromolecule immediately coprecipitate from solution forming said particles; and
 - c) isolating said particles from the organic solvent.
- 24. (Currently Amended) Biological macromolecule coated micro-crystals comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon wherein the coprecipitant has a molecular weight of less than 1,000 Da and is selected from the group consisting of

inorganic salts,
sugars, polysaccharides, carbohydrates, polyols, and derivatives thereof;
amino acids;
acid-base buffers;
zwitterionic compounds;
organic salts;
compounds containing multiple basic groups;

Appl. No.: 10/007,257 Filed: 11/12/2001

Page 6

compounds containing multiple acidic groups;

bile salts; and,

water soluble dyes;

polar or ionic polymers; and

polar or ionic dendrimers.

25. (Currently Amended) A pharmaceutical formulation comprising biological macromolecule coated micro-crystals comprising a coprecipitant core with a dehydrated pharmaceutically active biological macromolecule coated thereon wherein the coprecipitant coprecipitant has a molecular weight of less than 1,000 Da and is selected from the group consisting of

inorganic salts,

sugars, polysaccharides, carbohydrates, polyols, and derivatives thereof <u>with a molecular</u> weight less than 10,000 Da;

amino-acids;

acid-base buffers;

zwitterionic compounds;

organic salts;

compounds containing multiple basic groups;

compounds containing multiple acidic groups;

bile salts; and,

water soluble dyes;

polar or ionic polymers; and

polar or ionic dendrimers; and a suitable carrier therefore.

26. (Currently Amended) An inhalable pharmaceutical formulation comprising biological macromolecule coated micro-crystals comprising a coprecipitant core with a dehydrated pharmaceutically active biological macromolecule coated thereon wherein said coprecipitant has a molecular weight of less than 1,000 Da.

Appl. No.: 10/007,257

Filed: 11/12/2001

Page 7

- 27. (Currently Amended) Water soluble particles of less than 50 μm comprising a coprecipitant partially, substantially or crystalline core with a dehydrated biological macromolecule coated thereon wherein said coprecipitant has a molecular weight of less than 1,000 Da.
- 28. (Previously Presented) Water soluble particles comprising a coprecipitant core with a dehydrated bioligical macromolecule coated thereon, wherein the coprecipitant is selected from ionic salts, amino acids, zwitterionic compounds, organic salts, sugars and polysaccharides of a molecular weight of less than 1,000 Da.

29. (Cancelled)

- 30. (Currently Amended) Water soluble particles comprising a coprecipitant core coated with a dehydrated biological macromolecule wherein the coprecipitant has a melting point at atmospheric pressure greater than 95°C and a molecular weight loss of less than 1,000 Da.
- 31. (Currently Amended) A liquid suspension comprising water soluble particles comprising a coprecipitant core coated with a biological macromolecule wherein said coprecipitant has a molecular weight of less than 1,000 Da.
- 32. (Currently Amended) A method of purifying a biological macromolecule from additives or impurities comprising:
- a) dissolving a coprecipitant in an aqueous solution comprising the biological macromolecule and additive or impurity wherein the coprecipitant is selected from the group consisting of inorganic salts; sugars, carbohydrates, polyols, and derivatives thereof with a molecular weight less than 10,000 Da; amino-acids; acid-base buffers; zwitterionic compounds; organic salts; compounds containing multiple basic groups; compounds containing multiple acidic groups; bile salts; and, water soluble dyes wherein the coprecipitant has a molecular weight of less than 1,000 Da;

Appl. No.: 10/007,257 Filed: 11/12/2001

Page 8

b) admixing the biological macromolecule/ coprecipitant solution with an excess of a water miscible organic solvent or solvents, in which the additive or impurity is soluble, such that the coprecipitant and biological macromolecule immediately coprecipitate from solution forming a biological macromolecule coated particle comprising a core of coprecipitant;

- c) rinsing said particles with fresh water-miscible organic solvent; and
- d) isolating said particles.
- 33. (Currently Amended) Water soluble particles according to claim <u>1</u> 5 wherein the coprecipitant is trehalose.
- 34. (Currently Amended) Water soluble particles according to claim 1 5 wherein the coprecipitant is an amino acid selected from the group consisting of glycine and arginine.
- 35. (Currently Amended) The method according to claim <u>11</u> 10 wherein the coprecipitant is trehalose.
- 36. (Currently Amended) The pharmaceutical formulation according to claim <u>25</u> 24 wherein the coprecipitant is trehalose.
- 37. (Currently Amended) The pharmaceutical formulation according to claim <u>25</u> 24 wherein the coprecipitant is an amino acid selected from the group consisting of glycine and arginine.
- 38. (Currently Amended) The pharmaceutical formulation according to claim $\underline{28}$ $\underline{25}$ wherein the coprecipitant is trehalose.
- 39. (Currently Amended) The pharmaceutical formulation according to claim 28 25 wherein the coprecipitant is an amino acid selected from the group consisting of glycine and arginine.

Appl. No.: 10/007,257

Filed: 11/12/2001

Page 9

40. (Previously Presented) Water soluble particles according to claim 1 wherein said coprecipitant core is a non-polymeric core.

41. (Previously Presented) The method according to claim 6 wherein said coprecipitant core is a non-polymeric core.